

## **Unit 1: EMBRYONIC STEM CELLS LESSON**

### **IN VITRO FERTILIZATION AND EMBRYONIC DEVELOPMENT PREIMPLANTATION GENETIC DIAGNOSIS**

#### **CALIFORNIA STANDARDS:**

- 2d. Students know new combinations of alleles may be generated in a zygote through the fusion of male and female gametes (fertilization).
3. A multicellular organism develops from a single zygote, and its phenotype depends on its genotype, which is established at fertilization.

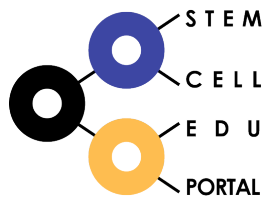
#### **GOALS:**

##### **Understand natural fertilization and in vitro fertilization**

Understand the stages of early development and how they relate to stem cells

#### **OBJECTIVES:**

1. The student will demonstrate an understanding of the difference between natural fertilization and in vitro fertilization.
2. The student will be able to differentiate between the morula and the blastocyst and understand how each relates to embryonic and fetal development.
3. The student will be able to explain the in vitro fertilization procedure in general terms from ovulation induction through embryo transfer.
4. The student will be able to describe the origin of pluripotent stem cells (inner cell mass) and their importance in medicine. Students will distinguish between totipotent and pluripotent stem cells.
5. The student will be able to describe how embryonic stem cell lines are developed.
6. The student will be able to explain preimplantation genetic diagnosis (PGD).
7. The student will be able to recognize areas of debate regarding the ethics of preimplantation genetic diagnosis and stem cell research.



## **RESOURCES and APPENDICES**

Embryonic stem cell and embryonic development background Information

*Northwest Association for Biomedical Research*

[http://www.nwabr.org/education/pdfs/StemCell/Stem\\_Cell\\_Handout.pdf](http://www.nwabr.org/education/pdfs/StemCell/Stem_Cell_Handout.pdf)<sup>1</sup>

University of New South Wales Embryology Foundations lecture by Dr. Mark Hill

<http://embryology.med.unsw.edu.au/Medicine/FlectureEmbryo.htm>

Introductory PowerPoint “Stem Cells and Regenerative Medicine” presentations:

[http://www.cirm.ca.gov/Stem\\_Cell\\_Modular\\_Units](http://www.cirm.ca.gov/Stem_Cell_Modular_Units)

## **APPENDICES**

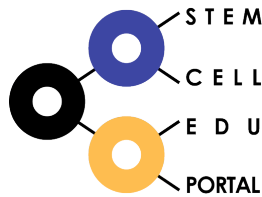
All appendices can be downloaded from: [http://www.cirm.ca.gov/curriculum\\_unit-1](http://www.cirm.ca.gov/curriculum_unit-1)

- A. Diagrams and handouts on in vitro fertilization
- B. Sea Urchin Development Microscope Lab and Part B: Human Development (student worksheets)
- C. Play Dough Models—similar to p.38-43 of the Northwest Association for Biomedical Research “The Science and Ethics of Stem Cell Research” curriculum available online at <http://www.nwabr.org/education/stemcellforum.htm> -- (student worksheets and handouts)
- D. In Vitro Fertilization (student worksheet and assessment with teacher answer sheet)

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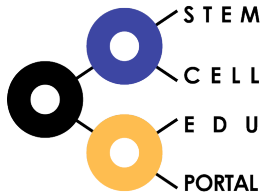
<sup>1</sup> These materials were developed by the Northwest Association for Biomedical Research (NWABR). Additional information and curriculum are available on their website at [www.nwabr.org](http://www.nwabr.org).

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#### E. Jigsaw exercise references

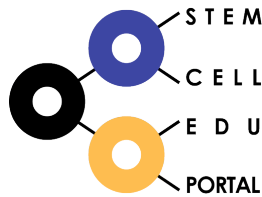
- a. Thompson article "Embryonic Stem Cell Lines Derived from Human Blastocysts". Thomson, James A., Joseph Itskovitz-Eldor, Sander S. Shapiro, Michelle A. Waknitz, Jennifer J. Swiergiel, Vivienne S. Marshall, and Jeffrey M. Jones. "Embryonic Stem Cell Lines Derived from Human Blastocysts." *Science* 282 (November 1998): 1145-1147.  
<http://www.sciencemag.org/cgi/content/full/282/5391/1145> Summary:  
[http://www.cirm.ca.gov/files/images/Education\\_portal/unit\\_1/Thomson%201998%20summary\\_072009.doc](http://www.cirm.ca.gov/files/images/Education_portal/unit_1/Thomson%201998%20summary_072009.doc)
- b. Damewood article "Ethical Implications of a New Application of Preimplantation Diagnosis. Marian D. Damewood. "Ethical Implications of a New Application of Preimplantation Diagnosis." *JAMA*. 2001;285(24):3143-3144. <http://jama.ama-assn.org/cgi/content/extract/285/24/3143>
- c. Klimanskaya et al. article "Human Embryonic Stem Cell Lines Derived from Single Blastomeres". Klimanskaya, Irina, Young Chung, Sandy Becker, Shi-Jiang Lu, and Robert Lanza. "Human embryonic stem cell lines derived from single blastomeres." *Nature* 444 (November 2006): 481-485. Summary: [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Summary\\_Lanza.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Summary_Lanza.pdf)
- d. Vastag article "Merits of Embryo Screening Debated" Brian Vastag. "Merits of Embryo Screening Debated." *JAMA*. 2004;291(8):927-929. <http://jama.ama-assn.org/cgi/content/extract/291/8/927>
- e. Finkel article "Stem Cells Without Killing Embryos". Elizabeth, Finkel. "Stem Cells Without Killing Embryos." *Cosmos Magazine* 2007 Web. 16 Jul 2009. <http://www.cosmosmagazine.com/news/1398/stem-cells-without-killing-embryo>
- f. American Society for Reproductive Medicine (ASRM) Fertility and Sterility article "Preimplantation Genetic Testing: a Practice Committee Opinion" "Preimplantation Genetic Testing: a Practice Committee Opinion." *Fertility and Sterility* 90(2008): S136-143.  
[http://www.asrm.org/Media/Practice/Preimplantation\\_genetic\\_testing.pdf](http://www.asrm.org/Media/Practice/Preimplantation_genetic_testing.pdf)  
(can only be read electronically, not printed) Summary:  
[http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Summary%20PGD.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Summary%20PGD.pdf)



- g. (Optional article) ASRM paper on the number and uses of cryopreserved embryos in U.S. David I. Hoffman, M.D., Gail L. Zellman, Ph.D., C. Christine Fair, M.A., Jacob F. Mayer, Ph.D., Joyce G. Zeitz, B.Sc., William E. Gibbons, M.D., and Thomas G. Turner, Jr., M.S. "Cryopreserved embryos in the United States and their availability for research." *Fertility and Sterility* 79(5) May 2003. 1063-1069.  
[http://www.asrm.org/Professionals/Fertility&Sterility/cryoembryos\\_may2003.pdf](http://www.asrm.org/Professionals/Fertility&Sterility/cryoembryos_may2003.pdf) (printable) Summary: [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit1\\_Summary\\_Authors.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit1_Summary_Authors.pdf)
- F. Preimplantation Genetic Diagnosis (PGD) Policy Options (application student worksheet)
- G. In-Vitro Fertilization and Embryonic Development Assessment

***Other resources for this lesson***

- Computer graphics and YouTube clips (see Bibliography for urls)
- Search for additional free scientific articles on Google Scholar:  
[www.google.com/scholar](http://www.google.com/scholar)
- Additional resources from Northwest Association for Biomedical Research website <http://www.nwabr.org/education/stemcell.html>



## ***Lesson Background:***

### **EMBRYONIC DEVELOPMENT**

Day 0: Fertilization of egg with a sperm

D ~0.5: Genetic bundles called “pronuclei” from mom and dad fuse to form the zygotic nucleus.

Day 1: ZYGOTE divides into 2 cells (EMBRYO)

Day 2: 4-cell EMBRYO

Day 3: 8-cell MORULA (“morula” refers to the berry-like shape of the early embryo)

Day 4: 16, 32, 64-cell MORULA

Day 5: Formation of hollow BLASTOCYST with embryonic stem cells and trophoblast

Days 7-14: Uterine implantation

Day 14: Gastrulation - three distinct layers begin to form (no more embryonic stem cells)

Days 14-21: Neurulation - beginning of future nervous system

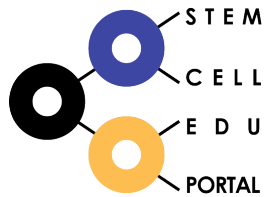
Days 21-24: Beginning of future face, neck, mouth, and nose

Weeks 3-8: Beginning of organ formation (organogenesis)

Week 8: Now it’s called a FETUS (definitions of this timepoint vary, up to 10 weeks.)

### **INFERTILITY AND TREATMENTS**

Infertility is a disease defined by the failure to achieve successful pregnancy after 12 or more months of regular unprotected intercourse. There are many reasons why sex may not result in a viable pregnancy. Biological dysfunctions at the genetic, cellular, and systems level within a man, woman, or both can prevent sperm and egg from combining and developing into a healthy baby. A man might have a low sperm count (oligospermia) or produce semen without sperm; his sperm might be irregularly shaped and have motility problems; his sperm might have trouble attaching to the egg; or he might have a blockage in his reproductive tract that prevents ejaculation. A woman might not be producing an egg because she may not be ovulating properly, possibly due to abnormal hormone levels (estrogen, progesterone, or prolactin) crucial for maintaining a menstrual cycle and a pregnancy. Or, the egg might be blocked on its path from the ovaries through the fallopian tubes to the uterus. Blockages can be caused by inflammation in the fallopian tube due to menstrual **cytokines** (small molecules that cause an inflammatory response) or infection. Uterine scarring, cysts, or an abnormally-shaped uterus could prevent an embryo from implanting correctly. Additionally, even if sperm and egg are able to combine, a chromosomal abnormality (**aneuploidy** or **translocation**) in either or both gametes may disrupt cell division and prevent further development.



Environmental factors, notably cigarette smoke, contribute to infertility. The percentage of women experiencing a 12 month (or more) conception delay was 54% higher in smokers than non-smokers. Chemicals in cigarette smoke have direct mutagenic effects (cause DNA damage) on egg cells. These chemicals have a variety of effects on female reproduction, such as a shorter menstrual cycle, accelerated follicular depletion, and earlier age of menopause. Male smokers experience a 22% average decrease in sperm production as compared to non-smokers. Smoking may have adverse affects on sperm function as well. Second-hand smoke contributes to infertility almost to the same degree as first-hand smoke.

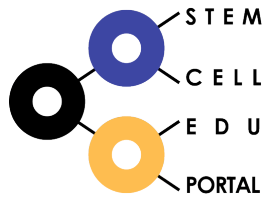
**In vitro fertilization (IVF)** is a procedure that couples may use when one or both of the partners are diagnosed with infertility. For couples in which one or both partners have a genetic disease, regardless of infertility, IVF can increase the chances of having a child without the disease. In the latter, early embryos created by IVF undergo a procedure called **Preimplantation Genetic Diagnosis (PGD)**, in which one **blastomere** (cell) is removed and its DNA tested for identifiable genetic disorders or chromosome abnormalities. “Disease-free” embryos can then be chosen for transfer into the uterus. Alternatives to IVF are adopting an IVF embryo from another couple, paying a sperm or egg donor to achieve in vitro fertilization with one parent’s gametes, and adopting or parenting a child.

## IN VITRO FERTILIZATION PROCEDURE

In vitro fertilization has several parts. Before the procedure begins, the parents are tested for infertility. Then, they must sign informed consent documents before they move on to the treatment. Egg maturation, egg collection, egg culture, sperm collection, in vitro fertilization, embryo culture, embryo selection, and embryo transfer are all part of the IVF procedure.

If a couple is investigating IVF as a treatment option, basic screening tests are performed to make sure the woman has a sufficient “ovarian reserve.” Follicle Stimulating Hormone (FSH) produced by the anterior pituitary acts as a signal to the ovaries to produce the hormone Estrogen and mature follicles. Follicles are sacs of cells and fluid encompassing a single growing ovum. Mature follicles are about 20mm in diameter, the size of a small grape, before the primary follicle bursts, releasing the egg into the fallopian tube.

Levels of FSH tend to increase as a woman gets older, as it takes more of this hormone to promote follicle development with age. Therefore, a doctor will test the level of FSH around day 3 (at the beginning) of a woman’s natural menstrual cycle. A lower FSH



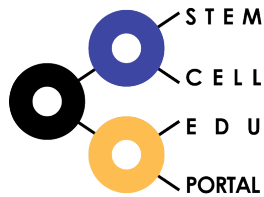
level is better, as a higher level may indicate poor egg quantity and quality. Another test for a woman's ovarian reserve (her reproductive potential) is the number of **antral** follicles remaining in her ovaries. The number of antral follicles strongly correlates with the number of primordial eggs, which have the potential to mature into ova ready for fertilization. The number of antral follicles can be determined by vaginal ultrasound, and having more follicles is better. Advanced age can contribute to a low ovarian reserve, and test results indicating this may convince a doctor to discontinue the IVF procedure. Tests performed on the man would indicate sperm count, motility, and **morphology**. If these factors were low or abnormal, a couple may opt to proceed with a modified IVF procedure called **Intracytoplasmic Sperm Injection (ICSI)**, explained below.

Once these tests are complete, both partners must sign consent forms which clearly explain the risks of the medical procedures to them and their future child/children. Risks include Ovarian hyperstimulation syndrome, an exaggerated response to **exogenous gonadotropins** that can lead to serious and life-threatening illness; discomfort, bleeding, or injury to organs near the ovaries; pelvic infection which may lead to removal of infected ovaries or tubes; multiple pregnancy which can affect the babies' health; and **ectopic** pregnancy, where the embryo implants outside the uterus often leading to spontaneous abortion. Besides the physical risks, there are psychological risks that come with a failed procedure.

The entire IVF procedure, from the beginning of hormone treatments through embryo transfer, takes approximately 24 days. A regimen of hormone injections is designed to stimulate the woman's ovaries to overproduce mature follicles. These hormones include: agonists and antagonists of Gonadotropin Releasing Hormone (GnRH) that delay the LH surge and ovulation to allow time for many mature follicles to develop; FSH to stimulate the development of multiple follicles; and Human Chorionic Gonadotropin (hCG) to induce final maturation of the eggs. These **subcutaneous** injections are self-administered, totaling up to twice per day for 17 days, and in addition estrogen and **progesterone** pills are taken longer-term to develop and maintain a uterine lining necessary for pregnancy.

After this ovarian stimulation and once the eggs are mature, anesthesia is given and then an ultrasound-guided needle inserted through the vagina aspirates between 10 and 30 eggs from the mature follicles. On the same day, sperm is collected from the man. If his tests showed normal sperm counts, his semen is mixed with the eggs in a petri dish, fertilizing them. If his test results were abnormal, a doctor may use the ICSI procedure, where one robust sperm is sucked up into an injection pipette. While a holding pipette secures one egg in place, this "hand-picked" sperm is injected into the





center of the egg. This is repeated for all eggs. ICSI successfully fertilizes 50-80% of eggs, but this procedure may damage the eggs, prevent the fertilized egg from dividing, or prevent the embryo from growing. The long-term effects of ICSI on the health of children fertilized this way are unknown since the procedure was perfected in 1992.

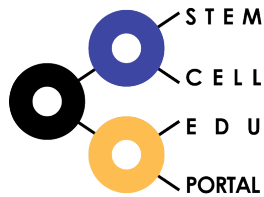
From here on, fertilized eggs produced by In vitro (“within the glass”) fertilization develop similarly to those produced by natural fertilization (in vivo, or “within the living organism,” fertilization). The only difference is the environment supporting development from fertilized egg (**zygote**) to blastocyst. In natural fertilization, this environment is the fallopian tube and the uterus. With IVF, this environment is a petri dish filled with drops of culture medium that mimics the natural environment. The petri dish is placed within an incubator, keeping the developing embryos at body temperature.

## EMBRYONIC DEVELOPMENT AND TRANSFER

In both natural and in vitro fertilization, the genome of the zygote is a unique combination of the haploid nucleus from the mother’s egg cell and the haploid nucleus from the father’s sperm cell. On day 1 post-fertilization, the zygote divides (mitosis) into two cells. On day 2, each of those cells divides, making four identical cells. On day three, the cells divide again, making eight cells (and so on). At this stage of embryonic development, the embryo is called a **morula**. The cells in the morula continue to divide, and on day 5, fluid builds up inside the ball of cells causing it to be hollow. At this stage, the embryo is called a **blastocyst**. The outside layer of the blastocyst, called the **trophoblast** (or trophectoderm), is made up of cells that attach to the uterine lining and eventually become the placenta. Inside the hollow ball, a clump of cells called the inner cell mass will eventually become the fetus. These cells are called **embryonic stem cells**, and they are **pluripotent** because they have the potential to specialize into every mature cell type *in the adult*. **Totipotent**—a property of the zygote (day 1) and every cell existing through the morula (day 3)—cells have the potential to become ALL types of cells in the mature adult and the trophoblast cells that develop into the placenta and extra-embryonic tissues. Thus, a totipotent cell could potentially make an *entire* human being, whereas a pluripotent cell could not because it has specialized past the point of being able to form trophoblast.

On day 5, the doctor chooses a few healthy-looking blastocysts out of the batch of 10-30 blastocysts (from the 10-30 harvested eggs) and transfers them into the woman’s uterus. Hopefully one (and preferably only one) will successfully implant into the uterine lining and continue developing. Typically, more than one embryo is implanted to increase the probability of a successful pregnancy and birth. However, there are specific





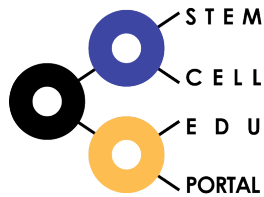
guidelines for the maximum number of embryos to transfer because multiple pregnancies can develop if more than one embryo successfully implants and develops. Multiple pregnancies may cause harm to the fetuses and the mother. According to the guidelines from the American Society for Reproductive Medicine, as the age of a woman undergoing IVF increases, the allowed number of embryos transferred increases. For example, women under 35 can have a maximum of one blastocyst transferred; women aged 35-40 can have two; and women over 40 can have up to three. Exceptions are if a woman has a poor prognosis—previous IVF attempts have been unsuccessful or the embryos are of poor quality—or if cleavage-stage embryos (up to the 8-cell stage) are used. In these cases more embryos (up to five in age 40+) can be transferred.

After the doctor has transferred the blastocysts, the leftover embryos are frozen at -80°C. In suspended animation, these frozen embryos can later be used by the couple if the pregnancy is unsuccessful or if they want to have more kids. They are often discarded. In a few cases, embryos are donated to another infertile couple for adoption. They can also be donated with consent to stem cell research. A scientist would aspirate the inner cell mass containing embryonic stem cells and plate them onto a petri dish to make an embryonic stem cell line. This destroys the embryo because it removes the pluripotent cells that would have developed into the fetus, leaving a shell of trophoblast cells that do not have the developmental capacity to replace the embryonic stem cells.

## PREIMPLANTATION GENETIC DIAGNOSIS

Preimplantation genetic diagnosis (PGD) is a procedure that allows a couple with or without infertility to know if their children have a chance of inheriting one or both of the parents' genetic diseases. Huntington's Disease is a **neurodegenerative** disease passed dominantly on to the next generation. For a carrier of Huntington's (Hh, who would manifest the disease), there is a 50% chance this person's child would have Huntington's. For two unaffected carriers of an **autosomal** recessive disorder, like Cystic Fibrosis, there is a 25% chance their child would manifest the disorder. Using IVF with PGD, a couple can see if of their embryos are carriers of disease alleles and then choose which of the embryos they want to transfer. In this procedure, one blastomere (or in some cases two) is removed from an 8-cell embryo. This does not damage the totipotent embryo; it continues to divide normally, quickly replacing the missing blastomeres.

To genetically test the cells, first Polymerase Chain Reaction would be used to amplify the amount of DNA for further analysis. One of the following techniques can be used to



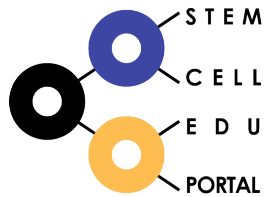
screen for disease alleles: **heteroduplex analysis** or **Fluorescence In Situ Hybridization (FISH)**. In heteroduplex analysis, specific DNA fragments containing genes responsible for a disease would be amplified from the unknown test sample and a known normal sample. Then the two would be hybridized, or mixed together so they are allowed to bind. A control sample is also made, containing hybridized DNA from two known normal samples. Mutations in the unknown DNA would cause irregularities in the shape of the hybridized DNA. After running **DNA gel electrophoresis** on the test and control samples, a difference in migration down the gel due to the slight shape differences in samples would indicate the presence of disease alleles. In the FISH technique, DNA probes attached to different-colored fluorescent molecules are allowed to bind to DNA sequences unique to each chromosome. These chromosomes can be examined under a fluorescence microscope for the number of each chromosome and for the presence of **translocations**. Down Syndrome is caused by the presence of three copies (trisomy) of chromosome 21 and can be identified by FISH.

## ETHICS OF PREIMPLANTATION GENETIC DIAGNOSIS

PGD gives couples with genetic diseases a chance to decide the genetic fate of their child. However, this decision comes with ethical challenges. For example, although some parents with Down Syndrome may not want their children to share their fate, some feel that their condition gives them a unique and valuable perspective on life and thus they disagree with selection against an embryo with Down Syndrome. Genetic “diseases” that society labels *abnormal* or that confer a *disability* can be thought of as natural biological variation, creating people with extraordinary characteristics and communities that support them. Conversely, the widespread ability to select for the genetic makeup of children could lead to a eugenic society (as in the movie *Gattaca*) filled with inherent inequalities.

On the other hand, PGD gives people with genetic disorders a chance to have “biologically related” children who are free of that particular disease, which some might consider a human right. In the future, techniques may be developed to make it easier to screen for multiple disease alleles using the DNA from one or two cells, creating opportunities for parents to lead a preventative lifestyle and help their children do so.

There is no conclusion on whether the rate of embryo implantation is affected by the PGD procedure. Chance of harm to the developing embryo is very small, 0.6%; normally, taking a cell from the morula does not disturb development. The diagnosis error of PGD for detecting translocation is approximately 10%. This includes chances of false negative, false positive, no result, and mosaicism. A mosaicism is when cells in



the embryo are heterogeneous in chromosomal makeup, for example because of a translocation during the early cell divisions. In this case all cells may not carry the genomic defect and there is a chance that the tested cell does have the defect while the other cells don't (and vice versa).

No single test can predict the risk of all gene variations in a child. Many conditions, such as those related to toxic exposure, are environmentally-based and are not detected with genetic testing. Additionally, in PGD there are risks to the mother inherent to the IVF procedure required for egg collection.

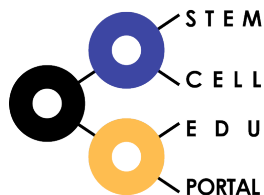
## REVIEWING THE CHARACTERISTICS OF EMBRYONIC STEM CELLS

Human embryonic stem cells are pluripotent cells derived from the inner cell mass of an IVF blastocyst. They have the ability to divide symmetrically (common in cell culture) as well as asymmetrically. During **asymmetric division**, a stem cell splits into two daughter cells—one remains a stem cell (**self-renews**) and the other changes into a more mature cell (**differentiates**). Depending on outside signals, an embryonic stem cell can differentiate into any of the 200+ cell types in the human body. This is medically important because scientists can direct the differentiation of these cells using combinations of chemicals to create any mature cells a patient needs. In development, the presence of embryonic stem cells persists until **gastrulation**, the formation of three germ layers in a 14-day-old embryo, after which adult stem cells appear. Adult stem cells (explained in Unit 2) can still divide asymmetrically, but differ from embryonic stem cells in that they are lineage-restricted and can only become certain types of cells in the adult body. Umbilical cord stem cells are a type of adult stem cell, but they may have some advantages over adult stem cells found in the tissues of the child and adult, with regard to reduced transplant immune rejection. Adult stem cells have incredible medical potential, as do embryonic stem cells, but come with fewer ethical concerns.

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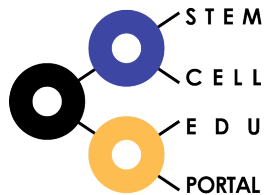
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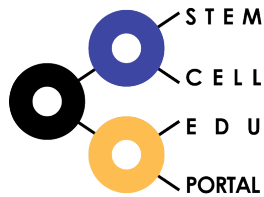
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## Glossary

**Aneuploidy:** having a chromosome number that is not a multiple of the haploid number

**Antral:** a cavity

**Asymmetric division:** produces two daughter cells with different properties

**Autosomal:** A chromosome that is not a sex chromosome

**Blastocyst:** hollow ball of cells containing an inner cell mass

**Blastomere:** any cell produced during cleavage

**Cytokines:** small molecules that cause an inflammatory response

**Differentiates:** the cell becomes more specialized

**DNA gel electrophoresis:** a technique used to separate DNA, RNA, and protein

**Ectopic:** occurring in an abnormal position or place

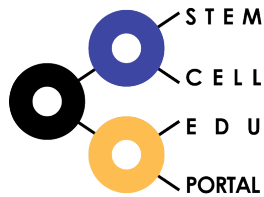
**Embryonic stem cells:** the inner cell mass of the blastocyst

**Exogenous:** derived externally

**Fluorescence In Situ Hybridization (FISH):** technique used to detect and localize the presence or absence of specific DNA sequences on chromosomes

**Gastrulation:** formation of a gastrula (the stage following the blastula)





**Gonadotropins:** follicle-stimulating hormone

**Haploid:** single set of chromosomes, i.e. half the normal diploid number

**Heteroduplex analysis:** electron microscope observation of duplex DNA formed by strands from different sources

**Intracytoplasmic Sperm Injection (ICSI):** an in vitro fertilization procedure in which a single sperm is injected directly into an egg

**In Vitro Fertilization (IVF):** a procedure that couples may use when one or both of the partners are diagnosed with infertility

**Morphology:** the study of form and structure of organisms

**Morula:** ball of eight cells

**Neurodegenerative:** relating to the degeneration of nervous tissue

**Pluripotent:** cells that have the potential to specialize into every mature cell type *in the adult*

**Preimplantation Genetic Diagnosis (PGD):** where one blastomere (cell) is removed and its DNA tested for identifiable genetic disorders or chromosome abnormalities

**Progesterone:** a hormone that prepares the uterus for the fertilized ovum and maintains pregnancy

**Self-renews:** remains the same kind of cell it began as before division

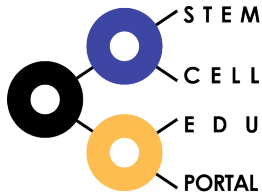
**Subcutaneous:** performed or introduced under the skin

**Totipotent:** cells that have the potential to become ALL types of cells in the mature adult *and* the trophoblast cells

**Translocation:** rearrangement of parts between genetically different chromosomes

**Trophoblast (or trophectoderm):** the outside layer of the blastocyst that eventually becomes the placenta and extra-embryonic tissues

**Zygote:** fertilized egg



## OUTLINE OF UNIT

### I. INVITATION:

#### A. ***Writing Activity: Assess pre-lesson knowledge***

1. Describe natural fertilization.
2. How did the “Octomom” become the mother of eight babies?
3. Draw what you think a five day-old human embryo looks like.

#### B. ***Discuss Octomom, the movie My Sisters Keeper***

Use the following as stimuli for discussion See Bibliography for web addresses to clips

View clips about Octomom in this order

1. OCTOMOM COMPLAINT
2. NADIA SULEMAN AND DRPHIL
3. NADIA ADMITS MISTAKE

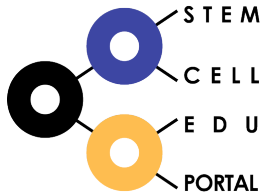
**View clips about My Sister’s Keeper in this order**

1. MYSISTERSKEEPER
2. WhatcanIDoForYou CLIP
3. INTERVIEW JODIPICOULT

### II. EXPLORATION

#### A. ***Natural Fertilization***

1. Lecture: Natural Fertilization - with graphic organizer “Human Fertilization and Development” (see Appendix A available for download at [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_A.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_A.pdf))
2. Animation of Human Development and Stem Cells (HHMI, at following link)  
[http://www.hhmi.org/biointeractive/stemcells/human\\_emb\\_dev.html](http://www.hhmi.org/biointeractive/stemcells/human_emb_dev.html)
3. Choose one of the lab activities below:



- a. Sea Urchin Embryology Lab:  
<http://www.stanford.edu/group/Urchin/>
  - b. Virtual sea urchin fertilization and development lab:  
<http://virtualurchin.stanford.edu/index.html>, click on fertilization and development to begin the interactive animation.
  - c. Sea urchin slides (Carolina catalogue #NP309702 Sea Urchin Development through blastula stage) and “Sea Urchin Development Microscope Lab” graphic organizer (see Appendix B, [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_B.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_B.pdf))
4. Play dough modeling activity – with graphic organizer “Draw Embryonic Development” (see Appendix C, [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_C.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_C.pdf)). Emphasize stages/sites at which totipotent and pluripotent stem cells occur.

## **B. *In Vitro Fertilization***

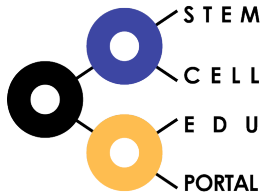
1. “In Vitro Fertilization” graphic organizer (see Appendix D, [http://www.cirm.ca.gov/curriculum\\_unit-1](http://www.cirm.ca.gov/curriculum_unit-1))
2. View CD film clips of IVF in this order (see Bibliography for urls):
  1. IVF and ICSI
  2. 3D animation of ICSI
  3. Intra-Cytoplasmic Sperm Injection
3. Assessment: Written comparison of natural and in vitro fertilization and description of locations of stem cells (see Appendix D, [http://www.cirm.ca.gov/curriculum\\_unit-1](http://www.cirm.ca.gov/curriculum_unit-1))

## **C. *Preimplantation Genetic Diagnosis and Stem Cells***

1. Discussion of characteristics of totipotent and pluripotent stem cells and formation of stem cell lines. Discuss ability of stem cells to differentiate, and how this is useful medically.

Use animation as stimulus for discussion (HHMI, or at following link)

[http://www.hhmi.org/biointeractive/stemcells/creating\\_lines.html](http://www.hhmi.org/biointeractive/stemcells/creating_lines.html)



How could scientists develop tissue for a patient? What are problems with transplanting foreign tissue into a patient? How might scientists get around this?

2. Jigsaw of articles activity/homework assignment: students assigned to read scientific journal articles, their scientific abstracts, or short summaries provided in Appendix E. Students can answer associated questions for homework; during class students get in “expert groups” to talk about questions, then break into “teaching groups” to share information from the articles listed. (See Appendix E [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_E.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_E.pdf) for full description of jigsaw activity and summaries)

**Group 1 reads:**

*Thompson: Embryonic Stem Cell Lines derived from Human Blastocyst*

**Group 2 reads:**

*Klimanskaya: Human Embryonic Stem Cell Lines Derived from Single Blastomeres.*

*Finkel: Stem Cells Without Killing Embryos.*

**Group 3 reads:**

*Damewood: Ethical Implications of a New Application of Preimplantation Diagnosis*

*Vastag: Merits of Embryo Screening Debated*

**Group 4 reads:**

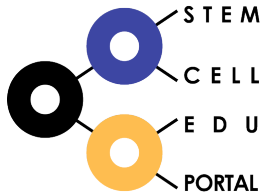
American Society for Reproductive Medicine: Preimplantation Genetic Testing: a Practice Committee Opinion

OPTIONAL Group 5 reads:

*Hoffman: Cryopreserved embryos in the United States and their availability for research.*

### **III. APPLICATION**

- A. Discuss ethics of Preimplantation Diagnosis after above jigsaw exercise, or in the context of a standalone lecture with discussion or policy forum.
- B. Finish with a ranking exercise – Review the following policy options for regulating preimplantation genetic diagnosis (from Vastag article) then ask students to rank these policy options using the “Preimplantation Genetic



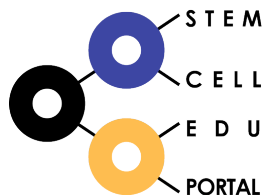
Diagnosis (PGD) Policy Options In-Vitro Fertilization and Embryonic Development Application” graphic organizer (Appendix F, [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_F.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_F.pdf))

Federal or state bans  
Legal limits passed by Congress

Professional Guidelines - regulations by doctors  
Status quo (parents and doctors decide to use PGD or not).

#### **IV. ASSESSMENT**

- A. Have students answer the following questions on the “In-Vitro Fertilization and Embryonic Development Assessment” (see Appendix G, [http://www.cirm.ca.gov/files/Education\\_Portal/Unit-1/Unit\\_1\\_Appendix\\_G.pdf](http://www.cirm.ca.gov/files/Education_Portal/Unit-1/Unit_1_Appendix_G.pdf))
1. Compare and contrast natural fertilization, in vitro fertilization, and in vitro fertilization with intracytoplasmic sperm injection.
  2. How do the morula and the blastocyst relate to embryonic and fetal development?
  3. How did the Octomom have eight babies?
  4. If Octomom and her doctors had followed the guidelines for the maximum number of embryos to be implanted, what could have happened to the remaining embryos?
  5. What are pluripotent stem cells and why are they important in medicine?
  6. Compare how scientists would derive a totipotent stem cell line from a morula versus a pluripotent stem cell line from a blastocyst.
  7. What is Preimplantation Genetic Diagnosis (PGD) and how might it help a family choosing in vitro fertilization?
  8. How do stem cells relate to PGD?
  9. What are some drawbacks of PGD?



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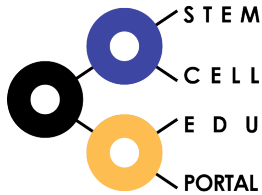
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Clips

## **YouTube**

“OCTOMOM COMPLAINT”

***NBC4 News Story, interview of Carole Lieberman:***

<http://www.youtube.com/watch?v=ykDwBYZmGyU>

“NADIA SULEMAN AND DRPHIL”

***Excerpt of Dr. Phil interview with Nadia Suleman:***

[http://www.youtube.com/watch?v=j7pX1k\\_mXb8](http://www.youtube.com/watch?v=j7pX1k_mXb8)

“NADIA ADMITS MISTAKE”

Showbiz Tonight coverage of Octomom:

<http://www.youtube.com/watch?v=eNpn1NslT0o&feature=related>

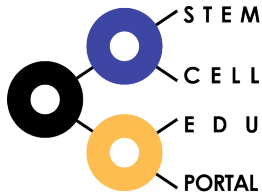
“MYSISTERSKEEPER”

***Official movie trailer:*** <http://www.youtube.com/watch?v=EdZZLdjBfCI>

“WhatcanIDoForYou CLIP”

Excerpt from My Sister’s Keeper movie:

<http://www.youtube.com/watch?v=GxMjxqQUpel&feature=channel>



## **“INTERVIEW JODIPICOULT”**

**Interview of Jodi Picoult:** <http://www.youtube.com/watch?v=2sLJ-sElZy8>

## **“IVF and ICSI”**

Dr. Murray from the Northern California Fertility Medical Center discusses IVF and ICSI:  
<http://www.youtube.com/watch?v=-OUEdLMrWN4>

“3D animation of ICSI”

**Schering-Plough production of the ICSI procedure:**

<http://www.youtube.com/watch?v=vGbIL9QWSsM>

“Intra-Cytoplasmic Sperm Injection”

Real-time footage of sperm being injected into egg:

<http://www.youtube.com/watch?v=oZ0cnrlJo5g&feature=related>

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“Creating embryonic stem cell lines”

[http://www.hhmi.org/biointeractive/media/creating\\_lines-lg.mov](http://www.hhmi.org/biointeractive/media/creating_lines-lg.mov)